

## **REMARKS/ARGUMENTS**

### ***Support for the Amendment***

The restrictions of the claims to nitric oxide as an analyte in exhaled breath and to the use of cytochrome-c in a sol-gel matrix as the sensing element are supported by the specification at page 4, lines 11-20, and the restriction to a nitric oxide concentration range of 5 to 200 ppb is supported at page 13, lines 24-28. Support for the recitation of an optical transducer in claim 19 is found in the specification at page 6, lines 6-9. Support for the recitation of the two sensing elements in claim 45 is found in the specification at page 12, lines 1-20. All other amendments are matters of clarification of the original wording.

Non-elected claims will be canceled when the elected claims are allowed.

### ***Claim Rejections -- 35 U.S.C. § 112, Second Paragraph***

The rejections under this section are addressed by the cancellation of claims 12-17 and the amendments to claims 18-21.

### ***Claim Rejections -- Double Patenting***

Application No. 10/334,625, cited in the double patenting rejection, received a Notice of Abandonment from the United States Patent and Trademark Office on September 7, 2006, thereby rendering the double patenting rejection moot.

### ***Claim Rejections -- 35 U.S.C. §§ 102 and 103***

As reflected in the amendments made herein to the claims, the invention is now restricted to a nitric oxide sensing device that utilizes a sensing element whose functional component is cytochrome-c in a sol-gel matrix, and that is able to detect nitric oxide at levels of 5-200 ppb.

Nitric oxide sensors made from cytochrome-c in a sol-gel matrix are known to undergo a detectable change when exposed to nitric oxide, and will then regenerate, i.e., return to their original condition ready for a fresh analysis, after the nitric oxide-containing atmosphere has been removed. The invention in these claims lies in applicants' discovery that when analyzing for nitric oxide at concentrations below 200 ppb, a cytochrome-c sensing element in a

sol-gel matrix is very slow to regenerate and is also much more sensitive to the presence of water than sensing elements designed for use at higher concentrations. While the obvious solution would be to control the water content by inclusion of a desiccant in the device, applicants have also discovered that to be useful a desiccant must have a water content that is controlled within a very narrow range. The problem faced by applicants is that desiccants cannot readily be controlled within such a narrow range and therefore will not result in a reusable sensing element. Once these discoveries were made, applicants realized that the solution is to use a disposable sensing element. This solution is not obvious since it was not previously known that it is only at these extremely low concentrations that cytochrome-c sensing elements do not regenerate to a sufficiently reliable degree to allow them to be re-used.

None of the four cited references, either alone or in combination, disclose the use of a sol-gel-suspended cytochrome-c sensor to detect nitric oxide levels below 200 ppb, and thus none face or recognize the same sensitivity issue or the slow regeneration problem. Gaston et al. US 6,033,368 describes a nitrogen oxide analyzer where the sensor is designed to respond to a breath condensate rather than a gaseous sample, and the detected amounts are in the ppm range rather than the ppb range. Aylott, *Chem. Mater.* **1997**, *9*, 2261-2263 likewise reports measurements only in the ppm range. Watson et al. US 5,831,742 addresses only carbon dioxide as an analyte, with no mention of the detection range or of regeneration or humidity. Bollinger et al. US 6,635,415 disclose a nitric oxide detector that does not involve cytochrome-c or a sol-gel. None of the sensitivity issues that are specific to these materials are present in the chemistry used by Bollinger et al.

**CONCLUSION**

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. Should any matters remain that can be resolved by a telephone conference, the examiner is encouraged to telephone the undersigned at 415-576-0200.

Respectfully submitted,



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